

Amendments to the Specification

Please replace paragraph [0007] of the Application with the following replacement paragraph:

-- [0007] The present invention provides a combination of carbon-13 and deuterium metabolic tracers and methods that when used in conjunction ~~conjunction~~ with nuclear magnetic resonance spectroscopy, provide a measurement of metabolic fluxes in the target organisms. --

Please replace paragraph [0017] of the Application with the following replacement paragraph:

-- [0017] The NMR method offers several advantages over mass spectroscopic analysis of glucose ^2H -enrichment. First, it does not require carbon-by-carbon degradation of glucose; rather, the relative ^2H -enrichment at each carbon position of glucose can be read out in a single ^2H NMR spectrum. Second, the prochiral H6R and H6S resonances are well separated in the ^2H NMR spectrum of monoacetone glucose so the normal assumptions required by mass spectrometry to quantitatively evaluate exchange at the level of fumarase in the TCA cycle are eliminated. This allows a separate measure of gluconeogenesis ~~gluconeogenesis~~ from the level of the triose phosphates (glycerol) *versus* PEP (the TCA cycle). Finally, the ^2H measurement is not compromised by the presence of ^{13}C -tracers so experiments can be designed to measure glucose production, gluconeogenic flux, pyruvate recycling flux and TCA cycle flux in a single experiment. --

Please replace paragraph [0038] of the Application with the following replacement paragraph:

-- [0038] It is important to point out that the ^2H NMR measurement is not influenced by the presence of tracer levels of ^{13}C in the glucose (or monoacetone glucose) molecule. Table 1 summarizes the relative contributions of glycogen, glycerol and PEP to glucose production as measured by deuterium NMR of monoacetone glucose derived from blood glucose. Fluxes through key pathways involving the TCA cycle were measured relative

to flux through citrate synthase by analysis of carbon-13 NMR spectra from urinary acetaminophen ~~acetaminophen~~ glucuronide or urinary phenylacetylglutamine. The equation (eqn) used to calculate a given value is indicated ~~indicated~~. --

Please replace paragraph [0041] of the Application with the following replacement paragraph:

-- [0041] The ^{13}C NMR spectra of urinary PAGN were also of high quality (Figure 6). Analysis of the glutamine C2 multiplets using eqns 7-9 provided the following relative flux estimates (Table 1): $\text{OAA} \rightarrow \text{PEP} = 6.3 \pm 0.4$; $\text{PEP} \rightarrow \text{pyruvate} = 5.4 \pm 0.4$ and $\text{PEP} \rightarrow \text{glucose} = 0.9 \pm 0.2$. As noted in an earlier study of 24-28 hr fasted individuals (21), flux estimates determined by analysis ~~analysis~~ of PAGN were significantly different from those derived from spectra of either blood glucose or urinary glucuronate. A comparison of the flux ratios derived from acetaminophen glucuronide and PAGN (Table 1) shows that PAGN reports a significantly lower relative $\text{PEP} \rightarrow \text{glucose}$ flux than reported by glucuronate ($p < 0.01$). There was no significant difference in estimates of $\text{PEP} \rightarrow \text{pyruvate}$ or $\text{OAA} \rightarrow \text{PEP}$ (relative to citrate synthase, Table 1). --

Please replace paragraph [0046] of the Application with the following replacement paragraph:

-- [0046] The data in TABLE 2 are fluxes through pathways supporting glucose production. The results of deuterium NMR analysis were used to calculate the rate of glucose production from PEP and other sources. The rate of production of PEP from the TCA cycle (in triose units) was indexed to flux ratios (calculated from either urine acetaminophen ~~acetaminophen~~ glucuronide or urine phenylacetylglutamine) in the TCA cycle to calculate absolute fluxes. The numbers in parenthesis refer to the numbered pathways in FIGURE 1. The abbreviation CS indicates citrate synthase. --

Please replace the Abstract of the Application with the following replacement Abstract:

-- The present invention provides a combination of carbon-13 and deuterium metabolic tracers and methods that when used in conjunction ~~conjunction~~ with nuclear magnetic ~~magnetic~~ resonance spectroscopy, provide a measurement of metabolic fluxes in the target organisms. The tracers of the present invention may be taken orally during the same clinical exam. The metabolic information can be derived from blood, urine or other fluids to provide a comprehensive profile of glucogenic metabolism. The subject matter of the present invention may be applied to the study of metabolic dysfunction related to obesity, diabetes, HIV infection and a variety of other disease conditions. --